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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/649,457	08/27/2003	Ronald G. Crystal	216474	5783

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EXAMINER	
NOBLE, MARCIA STEPHENS	

ART UNIT	PAPER NUMBER
1632	

MAIL DATE	DELIVERY MODE
12/23/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/649,457	CRYSTAL ET AL.	
	Examiner	Art Unit	
	MARCIA S. NOBLE	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 September 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,6-19,21 and 42-58* is/are pending in the application.

4a) Of the above claim(s) *2,3,11,12 and 42-58* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1, 6-10,13-19, and 21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Claims

1. Claims 1-3, 6-19, 21, and 42-58 are pending.

Election/Restrictions

2. Claims 2, 3, 11, 12, and 42-58 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected subject matter, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 4/24/06.

Claims 1, 6-10, 13-19, and 21 are under consideration.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

3. Claims 1, 6-10, 13-19, and 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gu et al. (1999, of record), Wu et al (1995; of record), Farina et al (2001, of record), Mogridge et al (2001; of record), and Hamdan et al (Parasitol Res. 88:583-586, June 2002, of record).

The instant invention is drawn to a chimpanzee replication-deficient adenoviral gene transfer vector comprising a nucleic acid sequence which encodes at least an immunogenic portion of protective antigen (PA) of *Bacillus anthracis* of SEQ ID NO: 1 and a heterologous sorting signal, lysosomal-associated membrane protein 1 (LAMP-1), wherein the nucleic acid sequence comprises codons expressed more frequently in humans than in *Bacillus anthracis*. Narrowing embodiments specify that the nucleic acid sequence encode an oligomerization mutant of PA, that the LAMP-1 direct the exotoxin to a lysosomal pathway, and that the gene transfer vector transduce antigen presenting cells (APC).

Gu et al teach a DNA plasmid vaccine encoding the immunogenic and biologically active portion of PA which encodes for AA 173-764 of PA (abstract and p. 341, col1, par 2), which encompasses the limitations of an immunogenic portion of PA. Therefore, the PA sequence taught by Gu et al encompasses the limitations of the instant claims. Gu et al also teach a need for the development of better anthrax vaccines that have improved safety profiles and immunogenicity and that do not trigger undesirable local reactogenicity (p. 340, col 2, par 1). Gu et al. do not teach a LAMP-1

sequence that direct the PA to the lysosomal pathway of APC cells, an adenoviral vector for delivery of the sequence, an oligomerization mutant of PA, nor codons that more frequently express in humans.

Wu et al teach a viral vector vaccine encoding the LAMP-1 signal peptide, the HPV16 E7 gene sequence and LAMP-1 sorting signal (par bridging 11671 and 11672, and Fig 1, on p. 11672). This vector was effectively expressed, and the chimeric protein was directed to the lysosomal compartments. Ultimately, the expression of the vector resulted in enhanced MHC II presentation of the E7 protein on APC (p. 11674, col 2, lines 4-11). Wu et al also teach that the use of a LAMP-1 sequence provides for improved vaccine potency and results in the production of potentially very effective vaccines (abstract, p. 11671, col 1 par 1, col2 par 2 &3, p. 1165 last par). Farina et al teach a replication-defective virus called C68 that was developed for gene transfer or as a vaccine carrier (see Materials and Methods for C68 disclosure). Farina et al also teach that this vector was generated to circumvent problems that arise because of existing immunity as a result of a naturally acquired adenoviral infection as seen with other vectors used for gene transfer or vaccine carrier (p. 11603 par bridging col 1 & 2, p. 1161, col 2 par 2). Farina et al also teach its improved utility as a vector because it does not result in neutralizing antibodies that can interfere with delivery (p. 11612, col 1, par 2). Farina et al also indicate that preliminary results indicate that the vector is functioning as an excellent vaccine carrier for HIV and rabies (p. 11612, last par).

Mogridge et al teaches a sequence encoding mutated form of amino acid sequence 510-518 of domain 3 of the PA that impair heptamerization of PA_{63} and are

also defective in their ability to bind LF and/or EF and therefore that these mutants are oligomerization deficient and result in impaired oligomerization necessary to the toxic effect of the exotoxins on cells (p. 2111, col 2 , par 2 and Table 1 p. 2113). This disclosure demonstrates the importance of domain three of PA in the function of all three exotoxins and there toxic impact on cells. It also provides motivation for use as a vaccine because it not only impairs the PA which is the most common target of anthrax vaccines. It also affects the other exotoxins involved and therefore targets the whole machinery of the toxin, therefore making it a more effective target for vaccine design.

Hamdan et al teach a method of redesigning *S. manosoni* cDNA using recursive PCR and preferred human codons without changing the amino acid sequence encoded by the gene of interest, SmGPCR (p. 584, col 1, par 1). Hamdan et al teach that this approach dramatically increased the expression of the gene in human HEK 293 cells and suggest that codon optimization is a valuable method for improving heterologous expression of non-human genes, more particularly bacterial genes, in human cells (see abstract).

At the time of the invention, it would have been obvious to an artisan of ordinary skill to modify the PA DNA vaccine taught by Gu et al to incorporate a LAMP-1 sorting signal taught by Wu et al and a viral vector as taught by Wu et al and Farina et al according to known recombinant DNA methods to predictably yield the instantly claimed PA DNA vaccine. It is acknowledged that the codon optimized sequence of SEQ ID NO:1 is not disclosed in the art. However, the process of codon optimization and specifically codon optimization of PA to improve the expression of an antigen in a

mammalian cell was established in the art, as exemplified by Mogridge et al and Hamden et al. Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to choose from a finite number of predictable codon optimized PA sequences, sorting signals, and viral vectors with a reasonable expectation of success of producing a functional DNA vaccine against PA as claimed. In summary, the art of Gu et al, Wu et al, and Farina et al demonstrate that the elements of the instantly claimed viral vector comprising a DNA vaccine against PA were established in the prior art and can be combined and codon optimized by molecular biology methods known in the prior art, as exemplified by Mogridge et al and Hamden et al. Therefore, the instantly claimed viral vector comprising a DNA vaccine encoding a codon optimized immunogenic portion of PA of SEQ ID NO:1 is rendered obvious by the art.

Applicant's arguments filed 9/18/2008 have been fully considered but they are not persuasive.

Applicant asserts that the cited references do not describe a finite number of predictable codon optimized PA sequences. Applicant states that the native PA sequence has 765 codons and these could be modified in thousands of possible ways. Therefore, it cannot be reasonably asserted that the prior art discloses a finite number of predictable codon optimized PA sequences for one of ordinary skill to systematically test let alone choose.

Applicant's argument is not found persuasive for the same reasons stated by Applicant. The PA sequence has 765 codons, which is a finite number of codons. Therefore, although it may be a vastly large number, there are only a finite number of permutations of the consequence that can be made. The art does not teach all of these permutations, but the art does teach a predictable means of making all of these permutations with a reasonable expectation of success. Therefore, contrary to applicant assertion, it would have been obvious to an artisan of ordinary skill that one could predictably arrive at the PA sequence of the instant claims using method routine in the art. Therefore, Applicant's arguments are not found persuasive and the instant rejection is maintained.

4. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MARCIA S. NOBLE whose telephone number is (571)272-5545. The examiner can normally be reached on M-F 9 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on (571) 272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Deborah Crouch/
Primary Examiner, Art Unit 1632

Marcia S. Noble